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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,292	03/29/2004	Dennis E. Discher	O-2863CIP	2280

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EXAMINER	
SILVERMAN, ERIC E	
ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
07/09/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,292	DISCHER ET AL.	
	Examiner	Art Unit	
	Eric E. Silverman, PhD	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,21 and 22* is/are pending in the application.

4a) Of the above claim(s) *21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10-29-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, filed 4/14/2008, has been received. Claims 1 – 16, 21 and 22 are pending.

Election/Restrictions

It is noted that in the response filed 10/29/2007, Applicants' elected doxorubicin as the encapsulant. New claims 21 and 22 require that the molecular weight of the encapsulant be greater than $1.0x10^5$ Da and less than $1.0x10^2$ Da, respectively. It is also noted that the election/restriction requirement mailed 8/27/2007 required Applicants to specify which claims read on the elected species, including any claims subsequently added. Doxorubicin has a molecular weight of 543 g/mol, which is neither greater than $1.0x10^5$ Da nor less than $1.0x10^2$ Da, and as such claims 21 and 22 do not read on the elected species. Irrespective of Applicants' failed to point out this out as required, the newly added claims 21 and 22 are **withdrawn** for reading on non-elected species.

As such, claims 1 – 16 are treated on the merits in this action and claims 21 and 22 are withdrawn from consideration.

Priority

Applicants' arguments with respect to the claim of priority to US 6,835,394 (issuing from Application 09/460,605) is noted. Applicants argue that the elected species of copolymer, PEO-butadiene block copolymer, is disclosed in col. 5, lines 15 – 21. The entire '394 patent has been reviewed, and special attention was paid to the segments noted in Applicants' response. Col. 5, lines 15 – 21 do not in fact disclose a PEO-butadiene block copolymer. This portion of the '394 patent discloses that block

copolymers are useful, and that any known polymer can make up the polymer block. The '394 patent then mentions non-limiting examples of monomers that could be used as blocks. Both polybutadiene block and a PEO block are mentioned, but there is nothing to indicate that the polybutadiene and PEO should be combined in a single block copolymer. At best, the '394 patent might make the elected species obvious. No analysis need be made as to whether the priority document does or does not make the elected species obvious because it is established that "[d]isclosure in an application that merely renders the latter-claimed (by amendment) invention obvious is not sufficient to meet the written description requirement of 35 U.S.C. 112, first paragraph." *Lockwood v. American Airlines, Inc.* 41 USPQ 2d. 1961 at 1966 (CAFC 1997) (emphasis added). If a Applicant's previous application (or patent issuing therefrom) does not meet the written description requirement of the claims in a later filed application, then the later application is not entitled to benefit of the filing date of the previous application. Because the '394 patent does not describe the instant claims within the meaning of 35 U.S.C. 112, first paragraph, the instant claims are not entitled to the benefit of the '394 patent's filing date. As such, the Discher reference is competent prior art against the instant application under one or more sections of 35 U.S.C. 102.

Information Disclosure Statement

The Examiner regrets the error in previously noting reference 96 (*Piskins et al.*) as not being reviewed. A new copy of the portion of the PTO/SB/08A listing this reference is included with this action. The copy included with this action indicates that the *Piskins* reference was considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 – 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4 recite “high molecular weight”, which is an indefinite term.

Claim 6 requires “increasing the mol %” of one of the components blended to "directly control release" of the encapsulant. As previously noted (see office action mailed 1/10/2008) it is not clear if this step means increasing the amount of the hydrolytically degradable monomer within the block copolymer is increased (for example, increasing the mol percent of hydrolytically degradable monomer within the block copolymer from 10 mol % to 20 mol %) or if this claim means increasing the amount of the entire copolymer that contains the hydrolytically degradable block copolymer with respect to the mol % of the other materials that are added or blended in the process. Further, it is not clear when or how the "increasing" step is performed. Based on the specification, it does not appear that the amount of any component of the vesicle can be increased after the vesicles are formed. But during the manufacture of the vesicle, the added hydrolytically degradable block copolymer is added as part of the “blending” step (as per claim 1). As such, it is not clear if or how the “increasing” step is different from the “blending" step.

The remaining claims are rejected for ultimately depending on one or more of the abovementioned claims without rectifying these issues

Response to Arguments

Applicants' arguments were fully considered, and were partially persuasive. With respect to the recitation of "high molecular weights" the arguments were not persuasive. Applicant argues that paragraphs 72, 77, and table 1 disclose appropriate molecular weights of PEG for the invention. In response, nowhere does the specification limit "high molecular weight" to any actual molecular weight range, or minimum. The artisan would not know if the molecular weights of Table 1 (for example) are "high" as claimed, or if they are merely "moderate" or "low". Nor would the artisan know what molecular weights are "high". Thus, the artisan would be completely unable to determine the scope of the instant claims. With respect to claim 6, the amendment to the claims mooted the portion of this rejection that related to the differences between mol % and mol fraction. However, the other reasons for this rejection discussed in the Office Action of 1/10/2008 still apply.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 – 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Piskin et al. in J. Biomater. Sci. Polymer Edn., in view of Won et al., Science 1999, and Discher et al., J. Phys. Chem. B for reasons of record and those discussed below.

Response to Arguments

Applicants' arguments have been fully considered, but they are not persuasive. Applicants argument that Discher is not competent prior art was discussed above under the heading "Priority". Applicants then argue that the claimed polymersomes do not require esterification for assembly, whereas, according to Applicant, this is required by the prior art. In response, it is noted that the instant claims use "comprising" language, which allows for additional steps, such as esterification. Nor is an esterification step forbidden by the instant claims. Applicants' next argue that there is a difference in mechanism of release between the invention of the instant claims and that of the art. This argument is not well understood. The instant claims are drawn to a process, not a product or composition of matter. It is not clear how an analysis of a composition of matter disclosed in the prior art is relevant to the patentability of process claims. To the extent that Applicants still believe this to be relevant, a further explanation of the relevance of the alleged distinctions would be helpful. Furthermore, the alleged differences in release mechanism are not recited by the claims, nor is it clear that they necessarily flow from the process of the instant claims. As an illustration, Applicants arguments is predicated on the claimed process making a material that exhibits poration at the membrane, yet the claims do not require that the material made by the claimed

process exhibit this property. Further, it is believed that this argument is a piecemeal analysis of Won, because it does not take into account Discher's explicit suggestion to blend PEG-PBD with another PEG-based block copolymer. Applicants continue by arguing that the Won reference teaches thick walled micelles, which are different from the thin walled micelles of instant claims. In response, it is noted that instant claims do not specify the wall thickness. As such, it cannot be said that they are of a different thickness than those of Won. Furthermore, the recitation of "thin-walled" is part of the preamble of the claim. Recitations in the preamble are only read as limitations when they are required to give life and breath to the claim. Here, in the absence of the preamble, the claim still recites a complete method. As such, the preamble is not required to give life and breath to the claim, and thus "thin walled" is not a functional limitation. Applicants then aver that Won's micelles lack a hydrolytic component. This argument is not well understood. Won teaches the use of the elected PEG-butadiene polymer in micelles. Applicants' argument is therefore best understood as an allegation that the elected PEG-butadiene copolymer is hydrolytic in the instant claims but not hydrolytic in Won. Because a product and its properties are not separable, this argument cannot be persuasive. If Applicants' believe that the Examiner has misunderstood this argument, then further explanation might be helpful. Applicants lastly argue that Discher does not teach selecting the appropriate blend of components, as per instant claims. In response, Discher clearly recognizes that PEG-PBD must be blended with another PEG-based polymer to be useful for drug delivery micelles. This is tantamount to a suggestion that the appropriate blend ratio should be determined in

order to tune the properties of the micelles generally, and in order to decrease the stability of PEG-butadiene specifically. Finding the optimal or working ratio in order to achieve the desired properties would be obvious, since that would be no more that routine optimization, or alternatively, finding the best or optimal conditions when the general conditions are known.

Finally, it is noted that Applicant's analysis of the references is piecemeal, while a proper analysis for obviousness must focus on what the references as a whole would have taught the artisan. The Piskin and Won references teach that PEG-PLA and PEG-PBD, respectively, are useful for forming micelles. According to Piskin, delivery from PEG-PLA micelles depends on degredation of PLA. While Piskin's micelles are suitable for drug delivery, Won's are not. Applicants' focus on this deficiency in Won, but fail to recognize that Discher suggests a solution to this problem. Specifically, Discher notes that PEG-PBD is unsuitable for drug delivery because it is too stable, but this problem can be overcome by blending PEG-PBD with other PEG-based block copolymers. Because PEG-PLA is a PEG-based block copolymer that is known to be suitable for drug delivery micelles, PEG-PLA is an obvious choice for blending with PEG-PBD. Because Piskin teaches that it is the PLA segment that controls the release of drug, the artisan would expect that the release rate could be controlled by determining the appropriate ratio of PLA containing copolymer (PEG-PLA) to PEG-PBD. Contrary to this straightforward reasoning, Applicant argument focuses on limitations that are not in the claims, such as the mechanism of release from Won or Discher's micelles, and the manner of assembly of the micelles, and alleged differences in

products described in the specification and those of the art when the instant claims are drawn to processes and not to products. Applicant also improperly focuses on perceived deficiencies in individual references without giving any consideration to the teachings of the three references as a whole. As such, Applicants arguments cannot be persuasive, and the rejection is still deemed proper.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is (571)272-5549. The examiner can normally be reached on Monday to Thursday 7:00 am to 5:00 pm and Friday 7:00 am to noon.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571 272 0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

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